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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,602	07/14/2000	CORINNE DEGERT	00108	8317

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,602	DEGERT ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-26,28-39 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-26,28-39 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request for the extension of time and filing of RCE both dated 10-10-03 are acknowledged.

Claims included in the prosecution are 22-26, 28-39 and 41.

Double Patenting

I. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 22-26, 28-34 and 41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 5,908,697. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant generic 'surfactant' includes the specific surfactant recited in the claims of said patent.

3. Claims 22-26, 28-34 and 41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12 of U.S. Patent No. 6,277,404. Although the conflicting claims are not identical, they are not patentably

distinct from each other because instant generic liposomes encompass the liposomes recited with size ranges in the claims of said patent.

Applicants indicate their willingness to file terminal disclaimers. The rejections are maintained in abeyance.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 22-26, 28-39 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over CA 2133421 in view of Munechika (5,662,931), Woiszwillo (6,268,053), Haynes (5,015,483) by themselves or in combination.

As pointed out before, the Canadian patent discloses multimalellar vesicles containing stacked bilayers and made from both ionic and non-ionic surfactants. The vesicles contain either hydrophobic or hydrophilic active agents and also contain a polymer (polyacrylamide) (note page 2, line 12 through page 3, line 11, page 7, Examples and claims). What is lacking in CA is an explicit teaching of including a stabilizer for the hydrophilic drug or enzyme along with the drug or enzyme. CA also lacks a specific teaching of the hydrophilic drug to be an enzyme.

Munechika discloses multi lamellar liposomes containing lecithin, a surfactant and enzymes such as urokinase. The liposomes further contain, stearylamine, cholesterol and an antioxidant. Munechika also discloses the incorporation of polymers

such as albumin, dextran, gelatin and others as stabilizers for the proteins and enzymes (note the abstract, columns 2-3, Examples).

Woiszwillo while disclosing micro particles encapsulating protein hormones and enzymes teaches that protein stabilizers such as glycerol, fatty acids, sucrose (a polyol) or any other protein stabilizers known to those skilled in the art may be added to the proteins prior to the formation of the micro particles to prevent denaturation (note col. 8, lines 20-33; col. 9, lines 4-8).

Haynes while disclosing liposomal compositions containing oxidizable active agents teaches the incorporation of oxygen scavengers such as enzymes and ascorbic acid to stabilize the oxidizable active agents (abstract and claims).

Encapsulation of a stabilizer such as albumin, gelatin, or a polysaccharide along with the protein or enzyme active agent in the multi lamellar vesicles of CA or WO would have been obvious to one of ordinary skill in the art since Munechika teaches that these compounds stabilize the drugs such as urokinase and Woiszwillo suggests the addition of stabilizers such as glycerol, fatty acids, sucrose (a polyol) or any other protein stabilizers known to those skilled in the art to proteins and enzymes prior to encapsulation. One skilled in the art would be motivated further to encapsulate the active agent together with the stabilizing agent since Haynes teaches such a combination would stabilize the oxidizable active agents.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments with regard to CA and WO have been fully addressed above. Applicant argues that Munechika discloses that tocopherol is used for stabilizing the lipid, and not for stabilizing a specific active ingredient in the liposomes and that there is no disclosure or suggestion that the active agent in the molecule is a reducing molecule, an oxidizing molecule or a molecule sensitive to hydrolysis which would need to be stabilized. This argument is not found to be persuasive. As pointed out above, Munechika teaches proteins as active agents and one of them is urokinase.

It is well known in the art that enzymes are susceptible to both chemical and enzymic hydrolysis and in instant claim 35 applicants themselves claim enzymes as the active agent. Applicants argue that while albumin may otherwise be known as a stabilizer, for certain enzymes, Munechika does not disclose this. Applicants are incorrect in stating so; the examiner points out col. 3, lines 8-11 teaches stabilizers such as albumin, dextrans, vinyl polymers, nonionic surfactants, gelatin and hydroxyethyl starch, the same compounds applicants themselves are claiming as evident from claim 37. Applicants' arguments that Munechika liposomes are different are not persuasive since these compounds would stabilize enzymes and protein irrespective of the type of liposomes and applicants have not shown otherwise.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is 703 308 2440. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703 308 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK